

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference <b>LO619.70003</b>	<b>FOR FURTHER ACTION</b>		See item 4 below
International application No. <b>PCT/US2004/043950</b>	International filing date ( <i>day/month/year</i> ) <b>29 December 2004 (29.12.2004)</b>	Priority date ( <i>day/month/year</i> ) <b>30 December 2003 (30.12.2003)</b>	
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237			
Applicant <b>THE BRIGHAM AND WOMEN'S HOSPITAL, INC.</b>			

<ol style="list-style-type: none"> <li>1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).</li> <li>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</li> </ol> <p>In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.</p>																								
<ol style="list-style-type: none"> <li>3. This report contains indications relating to the following items:           <table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 15%;"><input checked="" type="checkbox"/></td> <td style="width: 15%;">Box No. I</td> <td>Basis of the report</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table> </li> <li>4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).</li> </ol>	<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input checked="" type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input checked="" type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input type="checkbox"/>	Box No. VIII	Certain observations on the international application
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<input type="checkbox"/>	Box No. VIII	Certain observations on the international application																						

<p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No. +41 22 338 82 70</p>	<p>Date of issuance of this report <b>03 July 2006 (03.07.2006)</b></p> <p>Authorized officer <b>Philippe Becamel</b> e-mail: pt12@wipo.int</p>
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# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

REC'D 11 MAY 2005

PCT/ISA/2005

PCT

To:

21/7

see form PCT/ISA/220

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

### FOR FURTHER ACTION

See paragraph 2 below

International application No.  
PCT/US2004/043950

International filing date (day/month/year)  
29.12.2004

Priority date (day/month/year)  
30.12.2003

International Patent Classification (IPC) or both national classification and IPC  
C07D333/40, A61K31/381, A61P35/00, G01N33/68

Applicant  
THE BRIGHAM AND WOMEN'S HOSPITAL, INC.

#### 1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application

#### 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

#### 3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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D-80298 Munich  
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Authorized Officer

Seelmann, I

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**Box No. I Basis of the opinion**

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1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.  
 This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:  
 a sequence listing  
 table(s) related to the sequence listing
  - b. format of material:  
 in written format  
 in computer readable form
  - c. time of filing/furnishing:  
 contained in the international application as filed.  
 filed together with the international application in computer readable form.  
 furnished subsequently to this Authority for the purposes of search.
3.  In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

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**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

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The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

the entire international application,  
 claims Nos. 1, 2, 24-100 (industrial applicability), 101-106, 110-113

because:

the said international application, or the said claims Nos. 24-100 relate to the following subject matter which does not require an international preliminary examination (*specify*):  
**see separate sheet**

the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

the claims, or said claims Nos. 1, 2 are so inadequately supported by the description that no meaningful opinion could be formed.

no international search report has been established for the whole application or for said claims Nos. 1, 2, 101-106, 110-113

the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	<input type="checkbox"/> has not been furnished <input type="checkbox"/> does not comply with the standard
the computer readable form	<input type="checkbox"/> has not been furnished <input type="checkbox"/> does not comply with the standard

the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

See separate sheet for further details

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2004/043950

**Box No. IV Lack of unity of invention**

1.  In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:
  - paid additional fees.
  - paid additional fees under protest.
  - not paid additional fees.
2.  This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
  - complied with
  - not complied with for the following reasons:

**see separate sheet**
4. Consequently, this report has been established in respect of the following parts of the international application:
  - all parts.
  - the parts relating to claims Nos.

**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes:	Claims	3, 5-113
	No:	Claims	1, 2, 4
Inventive step (IS)	Yes:	Claims	3, 5-113
	No:	Claims	1, 2, 4
Industrial applicability (IA)	Yes:	Claims	1-23, 101-113
	No:	Claims	

2. Citations and explanations

**see separate sheet**

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.  
**PCT/US2004/043950**

**Re Item III**

Claims 24-100 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

The initial phase of the search for claims 1 and 2 revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which parts of the claim(s) may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of the claim(s) is impossible. Consequently, the search and the examination have been restricted to the compounds of present claim 3 and 4. The subject-matter of claims 101-106 and 110-113 has only been searched in view of the scope of the compound claims.

**Re Item IV**

**Lack of unity of invention**

Claims 101-106 and 110-113 are not limited to the scope of the claimed compounds. The claimed activity as such is, however, already known in the art, a single general inventive concept between the claimed compounds and the assay and the kit for the use in relation with other compounds than those of the present application is not detectable. This single inventive concept is defined as "involving one or more of the same or corresponding special technical features", which serve to distinguish the current application from the prior art (establishes novelty) and are responsible for the inventive activity. An objection concerning the unity of the invention must be expected in the regional phase.

**Re Item V**

**1. PRIOR ART**

Reference is made to the following documents:

D1: EP-A-0 234 622

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.  
PCT/US2004/043950

D2: EP-A-1 176 139  
D3: US 2003/187002 A1  
D4: US 2002/042428 A1  
D5: WO 99/55682 A  
D6: WO 03/006047 A

**2. NOVELTY**

The subject-matter of claims 3, 5-113 is considered to be novel (Article 33(2) PCT). The essential structural difference between the claimed compounds and those of D1-D4 resides i.a. in the R2 substituent.

The subject-matter of claims 1 and 2 is at least anticipated by D1-D4 (Article 33(2) PCT), these documents represent only an arbitrary selection of the relevant prior art. D1-D4 disclose generic formula with overlapping definitions and examples falling within this overlap (cf. search report). According to page 58 (line 1-2) the compound of claim 4 was commercially available at the time of drawing up this application, therefore, novelty for this compound cannot be acknowledged.

**3. INVENTIVE STEP**

The subject-matter of claims 3-100 and 107-109 can be considered as involving an inventive step (Article 33(3) PCT). The document D5 is regarded as being the closest prior art to the subject-matter of these claims. It discloses HLA agonists and antagonists. The structures of the active compounds are, however, completely different from the presently claimed. The problem to be solved by the present invention is seen in the provision of further compounds with HLA activity. In view of the experimental part and the other information as given in the description, it can be assumed that this problem has been solved by the compound F15 (claim 4). The prior art D6 discloses further information which relates HLA-DM to HLA-DR. Due to the structural differences even the combined teaching of D5 and D6 would not motivate a man skilled in the art to arrive at the present invention.